REMARKS

The claims are 18-37, with claims 18-22 being independent. Claims 1-17 have been canceled without prejudice or disclaimer. Support for claims 18-37 may be found in claims 1-17. No new matter has been added.

Applicants have submitted an amended abstract, which Applicants believe addresses the Examiner's objection.

Applicants also submit herewith amendments (by strikeout and underlining) to the originally filed specification. Applicants submit that the amendments to the specification do not add new matter.

Description 4 in the specification has been amended in accordance with amendments made in co-pending U.S. Patent Appln. No. 10/509,078. Description 4 recites the organic reagents used in the diazotization/iodination reaction sequence described in original Description 4.

Certain discrepancies between the Descriptions provided and the laboratory notebook procedures (e.g., relating to work-up and purification procedures, and reaction handling) were noted in co-pending U.S. Patent Appln. No. 10/509,078 for which no changes to the specification have been made. For example, in Description 2, the procedure in the specification does not indicate that in the final purification step, the Biotage flash column was first loaded with dichloromethane. For Description 3, the laboratory notebook does not contain a recitation of the extra step of cooling the reaction mixture in an ice bath.

Applicants respectfully submit that because the above-noted Descriptions involve the conventional use of conventional reagents and/or routine experimental techniques to accomplish conventional transformations and/or purifications, one of ordinary skill in the art would be able to prepare the compounds of this invention without undue experimentation.

Previously pending claims 1-10, 13, 15, and 17 were rejected under 35 U.S.C. 112, second paragraph, claims 14 and 15 were rejected under 35 U.S.C. 112, first paragraph, claims 1-10, 13-15, and 17 were rejected under 35 U.S.C. 102(e), and claims 1-10, 13-15, and 17 we rejected under 35 U.S.C. 103(a). Applicants respectfully traverse these rejections.

Cancellation of claims 1-17 renders each of these rejections moot, however, Applicants will address these rejections to the extent that they apply to new claims 18-37.

Previously pending claims 14 and 15 were rejected under 35 U.S.C. 112, first paragraph. The Examiner considers the specification to be enabling for treating anxiety, depression, schizophrenia and mild cognitive impairment, however the Examiner alleges that the specification does not reasonable provide enablement for the remaining uses covered by these claims. Accordingly, Applicants understand that the Examiner would find claims 23-27 to be enabled.

Applicants respectfully submit that one of ordinary skill in the art would also be able to make and use the invention defined in claims 28-32. Support for the treatment of Alzheimer's disease using a 5-HT_6 receptor antagonist may be found in the documents listed in the IDS submitted herewith. Included in these documents is an abstract reporting pre-clinical data for a 5-HT_6 receptor antagonist compound (SB-742457: 3-phenylsulfonyl-8-piperazin-1-yl-quinoline, where the compound of the present application is a polymorphic form thereof), two citations from ClinicalTrials.org describing clinical studies using the same 5-HT_6 receptor antagonist compound in Alzheimer's disease and a December 2007 LSE announcement that includes a discussion of the outcome of these two trials.

Previously pending composition claims 13 and 17 were rejected on the basis that "regardless of initial form present since once in solution the polymorphic forms would be indistinguishable." Applicants respectfully submit that the characterization data presented for the identification of a sample of 3-phenylsulfonyl-8-piperazin-1-yl-quinoline as form III (claims 18-22) would require the compound to be in solid form. As a result, compositions which require the compound to be in solution would be, by definition, outside of the scope of claims 33-37.

Previously pending claims 1-10, 13-15, and 17 had been rejected under 35 U.S.C. 102(e) as allegedly anticipated by Ahmed (WO'580) and under 35 U.S.C. 103(a) as allegedly unpatentable over Ahmed. Applicants request reconsideration of the rejections under 35 U.S.C. 103(c) given that both Ahmed and the present application are assigned to the same entity, Glaxo Group Limited. Additionally, the Examiner states that Applicants need to show that the compound of Ahmed (WO'580, corresponding to U.S. Patent Appln. No. 10/509,078) is not the instant form by a comparison employing art-recognized techniques. However, the Examiner has already noted differences between the Forms I and II of Ahmed and the Form III of the present invention, indicating that Form III is a novel crystal form. Multiple other differences in the characterization data can be readily observed.

A comparison of the XRPD data for Forms I and II from WO'580 and the data for Form III in the subject application follows.

Comparison of the diffraction angles between 0-10 °2θ

Form I	Form II	Form III
6.84		
8.61		
	9.30	
	9.95	
		10.29
10.47		
		10.76
	10.99	

Comparison of the diffraction angles between 11-19 °2θ

Form I	Form II	Form III
		11.94
13.01		
	13.40	
		14.33
	14.63	14.61
		14.93
	15.03	
15.11		
15.50		
	16.04	16.02
16.24		
	16.47	
16.63		
		16.80
17.20		
		17.47
	17.93	17.92
18.00		
	18.19	
	18.73	
		19.13
	19.17	
		19.55
19.65		
		19.84

Comparison of the diffraction angles between 20-29 °2θ

Form I	Form II	Form III
		20.33
	20.69	
21.07		
		21.16
		21.36
	21.49	
21.66		
	22.12	
22.20		
22.62		
		23.33
	23.55	
23.99		23.96
		24.44
	24.59	
		24.67
	25.27	
		25.51
25.61		
26.12		26.12
26.76		
	27.03	
		27.13
		27.77
27.96		
		28.06
	28.22	
		28.35
	28.61	
28.86		
		29.23
	29.48	29.46
29.64		
	29.81	

Comparison of the diffraction angles between 30-39 °2θ

Form I	Form II	Form III
		30.06
30.26		
		30.35
	30.70	
30.85		
		31.27
31.31		

	32.05	
		32.35
32.60		
		32.66
33.08		33.08
	33.32	
33.70		
		33.77
	33.95	
34.35		
	34.39	
		34.49
	34.90	
		35.18
35.65		
	35.77	
	36.25	
		36.42
36.85		
	36.80	
		37.34
	37.60	
38.05		
	38.19	
		38.39
38.46		
	38.70	
	39.26	
		39.51

There is little overlap of the XRPD diffraction angles between these 3 crystal forms. Moreover, even a cursory visual comparison of the XRPD patterns of Figures 3 and 6 of WO'580 and Figure 3 of the subject application reveals that significant differences exist between these crystal forms. See attached sheet.

Accordingly, the presently claimed Form III polymorph of 3-phenylsulfonyl-8-piperazin-1-yl-quinoline is novel over the Form I and Form II polymorphs of 3-phenylsulfonyl-8-piperazin-1-yl-quinoline described in WO'580.

The Examiner further contends that should Ahmed not anticipate the claimed polymorph, the polymorph is nonetheless obvious. Applicants respectfully disagree.

Applicants respectfully submit that Ahmed fails to support a *prima facie* case of obviousness for the presently claimed polymorphic form. Applicants acknowledge that Ahmed discloses the novel compound 3-phenylsulfonyl-8-piperazin-1-yl-quinoline.

Ahmed also discloses two specific crystal forms of this compound. The present invention discloses a third crystal form of this compound. Ahmed does not disclose or suggest the crystalline form of 3-phenylsulfonyl-8-piperazin-1-yl-quinoline that provides the IR and/or Raman spectra/spectral peaks and/or XRPD pattern/diffraction data defined in the pending claims. Ahmed does not describe or suggest a method to prepare the presently claimed crystalline form and nothing in Ahmed provides the requisite motivation to alter the teaching therein in ways necessary to arrive at the crystalline form of the present invention. Moreover, Ahmed does not provide the basis of any expectation that the crystalline form of 3-phenylsulfonyl-8-piperazin-1-yl-quinoline, that is characterized by any of the IR and/or Raman spectra/spectral peaks and/or XRPD pattern/diffraction data defined in the pending claims, could or would exist.

The issue of patentability of novel crystalline forms has been specifically addressed by the CCPA and the Federal Circuit Court of Appeals, and in each case the court has held that new crystalline forms of known compounds are patentable and are not obvious over other forms of the known compound. (*In re Cofer*, 354 F.2d 664, 148 USPQ 268 (CCPA 1966), *In re Irani* 427 F.2d 806, 166 USPQ 24 (CCPA 1970), *In re Grose,* 592 F.2d 116, 201 USPQ 57 (CCPA 1979) and *Bristol-Myers Co. v. U.S. International Trade Commission*, 15 USPQ 2d 1258 (Fed. Cir. 1989, unpublished)).

In the determination of obviousness, consideration must be given to the "invention as a whole." Applicants respectfully submit that the new *form* of the compound, as defined by the characterizing IR, Raman, ^{13}C NMR, and/or XRPD data in the pending claims, is part of the present invention as a whole and is a factor which must be given weight in the Examiner's analysis (See *In re Cofer*, 354 F.2d 664,668, 148 USPQ 268, 271 (CCPA 1966)).

In re Cofer, 148 USPQ 268, 271 (CCPA 1966):

> The new form of the compound set forth in the claims is as much a part of the "subject matter as a whole" to be compared with the prior art as are other properties of the material which make it useful.

Moreover, the comparison of the XRPD data provided above indicates that the crystalline Forms I and II of the 3-phenylsulfonyl-8-piperazin-1-yl-quinoline of Ahmed and the crystalline Form III of 3-phenylsulfonyl-8-piperazin-1-yl-quinoline of the present invention are different.

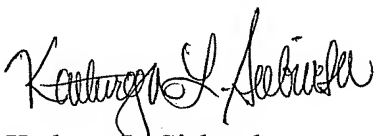
Applicants respectfully submit that the crystalline Form III of 3-phenylsulfonyl-8-piperazin-1-yl-quinoline defined in the pending claims is different from, and separately patentable over, the crystalline Forms I and II of 3-phenylsulfonyl-8-piperazin-1-yl-quinoline described in Ahmed (WO'580).

In re Grose, 201 USPQ 57, 63 (CCPA 1979):

> If the differences in X-ray diffraction data between the zeolites here involved had indicated an actual difference in crystal structure, the present record would belie a conclusion that such differences resulted from obvious modifications of any prior art synthesis process or from obvious modifications of Milton's zeolite R to yield the claimed zeolite.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the subject application is in condition for allowance. If the Examiner has any remaining objections or concerns, the Examiner is respectfully requested to contact Applicants' undersigned agent to resolve such issues and advance the case to issue.

Respectfully submitted,



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